REMARKS

Claims 1-37 had been pending and claims 1-11 were examined. Claims 12-37 have been withdrawn from consideration. Claims 2-4 and 7-11 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the cancelled subject matter in future applications. Applicants have amended claims 1, 5, and 6.

Claim 1 has been amended to recite steps. Support for that amendment is found in the specification as-filed, at least at page 2, lines 15-16 and 22 through page 3, line 6 and page 31, line 19 through page 32, line 9. Claims 5 and 6 have been amended to depend from claim 1, as claim 4 has been cancelled. In addition, claim 5 has been amended to correct a grammatical error. Thus, the amendments are fully supported by the application as filed. No new matter has been added. Upon entry of this amendment, claims 1, 5, and 6 will be under consideration.

Preliminary Matters

Information Disclosure Statement

The Office indicated that "[t]he Information Disclosure Statement filed 1 September 2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it is unsigned." Action at page 2.

Applicants note that the Information Disclosure Statement filed September 1, 2006, was submitted electronically. In compliance with 37 C.F.R. § 1.4(d)(2), Applicants' representative signed the Information Disclosure Statement using an S-signature. Enclosed is a copy of the IDS that was submitted electronically and that clearly shows the S-signature of Applicants' representative. Applicants respectfully request that the Office consider the IDS and initial next to each reference to indicate that they have been considered.

Claim Objections

The Office objects to claims 5 and 10 because of grammatical errors or informalities. Specifically, the Office states that "[i]n claim 5, it is believed that the phrase, 'Egr-1 depending renal disease' should read, 'Egr-1 dependent disease,'" and that "[i]n claim 10, the phrase 'under the control of transcriptional control by a protein' is grammatically incorrect." *Id.* at page 3.

As noted above, claim 5 has been amended to recite "Egr-1 dependent disease" and 10 has been cancelled. Applicants respectfully request withdrawal of the rejection.

Claim Rejections

Rejections under 35 U.S.C. § 112/101 - "use" claims

The Examiner rejected claim 1-6 under 35 U.S.C. § 101 "because the claimed recitation of a use without setting forth any steps involved in the process, results in an improper definition of a process." Action at page 4. The Examiner also stated that "[c]laims 1-6 provide for the use of a protein, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass." *Id.* at page 3.

Applicants respectfully traverse. Nonetheless, claim 1 has been amended to recite specific steps. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, first paragraph

Written description

Claims 1-11 were rejected under 35 U.S.C. 112, first paragraph as allegedly failing to comply with the written description requirement. According to the Examiner, "[t]he claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Action at page 4. Specifically,

the Examiner stated that the specification "does not provide adequate written description for the broad class of any polypeptide comprising substantially the same amino acid sequence as that represented by SEQ ID NO:1 and useful in a method of screening for a polypeptide and therapeutic substance associated therewith." *Id.* at page 8. The Examiner did however acknowledge that "the described polypeptides comprising SEQ ID NO:1 or SEQ ID NO:2 meet the written description provision of 35 U.S.C. § 112, first paragraph. *Id.*

Applicants respectfully traverse. Nonetheless, solely to facilitate prosecution and not in acquiescence to the Examiner's rejection, claim 1 has been amended to recite "the amino acid sequence of SEQ ID NO:2." Applicants therefore respectfully request withdrawal of the rejection.

Enablement

Claims 1-11 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. According to the Examiner, "[t]he claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Action at page 8. Relying on the *Wands* factors, the Examiner stated that "it would require undue experimentation to practice the invention claimed." *Id.* at page 13. Specifically, the Examiner stated that "the polypeptide of the claims is broadly drawn and, therefore, so too is the scope of the method of screening for a prophylactic and therapeutic substance for any disease associated with the protein." *Id.* at page 8 (emphasis original). The Examiner also stated that:

> [E]ven claims more narrowly drawn to screening for a prophylactic and therapeutic substance for renal disease or diabetic nephropathy cover the use of a wide variety of structurally and functionally diverse polypeptides in the method. Similarly, even if one were to construe claims limited to using an amino acid sequence represented by the recited sequence as requiring that the method

> use a polypeptide that comprises the recited sequence, the claims still embrace methods of identifying prophylactic and therapeutic substances for *any* disease associated with the protein.

Id. at page 9.

In addition, the Examiner urged that "the claims are directed to using the polypeptides of the claims as a marker for efficacy in the treatment of any disease associated in any way with the polypeptide." *Id.* at page 10. The Examiner then contended that "the art clearly teaches that the utility of a putative biomarker as an indicator of prophylactic and therapeutic efficacy is unpredictable and must be validated." *Id.* at page 11. The Examiner further alleged that "the application clearly does not contain validation of the method as it encompasses screening for a prophylactic and therapeutic substance that can be used to treat any disease associated with the protein of the claims." *Id.* at page 12. The Examiner concluded that "[c]ontrary to Applicant's assertions, there does not appear to be any evidence presented demonstrating that an agent that alters the expression or functions of Egr-1 produces a therapeutic effect in a disease model." *Id.*

Applicants respectfully traverse. Contrary to the Examiner's contention, the claims are not drawn to any polypeptide and any disease. Instead, the claims require a protein or salt thereof "comprising the amino acid sequence of SEQ ID NO:2." In addition, the claims require that the disease is a renal disease.

In response to the Examiner's contention that "there does not appear to be any evidence presented demonstrating that an agent that alters the expression or functions of Egr-1 produces a therapeutic effect in a disease model," Applicants also wish to make clear that the instant claims are drawn to a method of screening, as opposed to a method of treatment. Applicants also wish to point out that working examples are not required. The MPEP instructs that "[c]ompliance with the enablement requirement or 35 U.S.C. 112, first paragraph, does not turn on whether an

example is disclosed" and that "lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement." MPEP § 2164.02. Moreover, an "applicant need not have actually reduced the invention to practice prior to filing." *Id.* The Federal Circuit in *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 U.S.P.Q. 2d 1302, 1304 (Fed. Cir. 1987), further held that "[t]he mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it."

Nonetheless, the specification does provide a clear link between Egr-1 and renal disease. The specification provides at least three examples linking Erg-1 to a renal disease. First, using a well known model of diabetic nephropathy, Wistar fatty rats, Experimental Example 1 shows upregulation of Egr-1 in the kidney of animals with diabetic nephropathy. *See* Table 2. Furthermore, Experimental Example 5 shows that the expression of renal fibrosis-related genes, including tissue factor, fibronectin, and ICAM-1, increases upon Egr-1 over-expression in human fetal kidney cells. Moreover, Example 1 shows that antisense oligodeoxynucleotides specific to Egr-1, induce inhibition of tissue factor expression in rat glomerular mesangial cells. Thus, the specification clearly describes how to make and use the instant invention. For at least these reasons, Applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

"Claims 7, 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention." *Id.* at page 14.

Claims 7, 10, and 11 have been cancelled. Thus, this rejection is moot. Applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 102(b)

Claims 1-6

Claims 1-6 were rejected under 35 U.S.C. 102(b) "as being anticipated by any one of Rosenberg (1993) *Kidney Int.* 43:601-609, Rupprecht et al. (1993) *Am. J. Physiol.* 265:F351-F360 (hereinafter, Rupprecht '93), or Kim et al. (1995) *Circulation* 92:88-95 (made of record in the IDS filed 8 July 2004)." Action at page 15. Specifically, the Examiner stated that "Rosenberg et al. teaches comparing expression of Egr-1 mRNA in rat kidney (an indirect measure of protein expression) with and without infusion of various agents." *Id.* at page 16. The Examiner also stated that "Rupprecht '93 compares the production of Egr-1 mRNA in cultured mesangial cells in the absence of a test compound (i.e., PDGF only) to the production in the presence of a test compound (genistein)." *Id.* The Examiner further stated that "Kim et al. compares the production of Egr-1 mRNA in [the] carotid artery in the absence of a test compound (i.e., balloon injury only) to the production in the presence of a test compound (i.e., the angiotensin II receptor agonist TCV-116)." *Id.* The Examiner concluded that the method of each of the above documents "is the same as the method presently claimed." *Id.*

Applicants respectfully traverse. According to the M.P.E.P., "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 at 2100-67 (citing *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). Here, not one of Rosenberg, Rupprecht '93, or Kim describes each and every limitation of independent claim 1. For example, as acknowledged by the Examiner, Rosenberg performed *in vivo* infusion experiments in rats. Rosen stated that the purpose of his study was to "examine the in vivo effect of AngII on the renal expression of the early growth response genes *c-fos*, *Egr-1* and *c-jun*."

Rosenberg at page 601, abstract. Claim 1, however, requires, for example, *in vitro* steps of "cultivating a cell in the absence and presence of a test compound, wherein the cell is capable of producing a protein or salt thereof comprising the amino acid sequence of SEQ ID NO:2" and "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." Rosenberg does not disclose those steps nor does Rosenberg disclose a method of screening substances using an amino acid sequence of human Egr-1, i.e., SEQ ID NO:2. Accordingly, Rosenberg does not anticipate the instant claims.

Rupprecht '93 describes the mechanism of PDGF-induced Egr-1 expression in rat mesangial cells. However, Rupprecht '93 does not disclose all of the steps recited in claim 1. For example, Rupprecht '93 does not disclose a step of "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." Thus, Rupprecht '93 does not anticipate the instant claims.

Kim describes *in vivo* experiments examining angiotensin II type 1 receptor blockade in injured arteries in rats. Similar to Rosenberg and Rupprecht '93, Kim does not disclose each and every step of claim 1, including, e.g., *in vitro* steps of "cultivating a cell in the absence and presence of a test compound, wherein the cell is capable of producing a protein or salt thereof comprising the amino acid sequence of SEQ ID NO:2" and "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." Thus, Kim does not anticipate the instant claims.

For at least these reasons, not one of Rosenberg, Rupprecht '93, or Kim anticipate the instant claims. Applicants respectfully request withdrawal of the rejection.

Claims 1-7

Claims 1-7 were rejected under 35 U.S.C. 102(b) "as being anticipated by any one of Hofer et al. (1996) *J. Biol. Chem.* 271:28306-28310, Rupprecht et al. (1997) *Kidney Int.* 51:694-702 (hereinafter, Rupprecht '97), or Khachigian et al. WO 97/32979 (made of record in the IDS filed 8 July 2004)." Action at page 16. Specifically, the Examiner stated that "Hofer et al. compares the production of Egr-1 protein by cultured mesangial cells in the absence of a test compound to the production in the presence of various test compounds." *Id.* at page 17. The Examiner also stated that "Rupprecht '97 compares the production of Egr-1 protein by cultured mesangial cells in the absence of a test compound (i.e., PDGF only) to the production in the presence of various test compounds (i.e., antisense oligonucleotides)." In addition, the Examiner stated that "Khachigian et al. compares the production of Egr-1 protein by cultured mesangial cells in the absence of a test compound (i.e., serum only) to the production in the presence of a test compound (i.e., various oligonucleotides)." The Examiner again concluded that the method of each of the above documents "is the same as the method presently claimed." *Id.*

Applicants respectfully traverse. Not one of Hofer, Rupprecht '97, or Khachigian disclose each and every step recited by claim 1. Hofer, for example, describes experiments using antisense oligonucleotides to determine whether Egr-1 is required for mesangial cell proliferation. Hofer, does not describe steps of "cultivating a cell in the absence and presence of a test compound, wherein the cell is capable of producing a protein or salt thereof comprising the amino acid sequence of SEQ ID NO:2" or "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." Thus, Hofer does not anticipate the instant claims.

Rupprecht '97 examines the role of Egr-1 in glomerulonephritis using an *in vivo* rat model and various *in vitro* assays. Those *in vitro* assays, however, do not describe each and every step recited by claim 1. For example, they do not disclose a step of "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." Rupprecht '97, therefore, does not anticipate the instant claims.

Khachigian describes methods of inhibiting proliferation of cells. It does not, however, disclose steps of "cultivating a cell in the absence and presence of a test compound, wherein the cell is capable of producing a protein or salt thereof comprising the amino acid sequence of SEQ ID NO:2" or "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." For at least this reason, Applicants respectfully request withdrawal of the rejection.

Claims 1-10

Claim 1-10 were rejected under 35 U.S.C. 102(b) "as being anticipated by any one of Einstein et al. WO 01/04356 A1 or Alberini et al. WO 01/74298 A2 (both made of record in the IDS filed 8 July 2004)." Action at page 17. The Examiner alleged that "Einstein et al. teaches methods of identifying agents that modulate the activity of an Egr-1 protein including comparing protein expression in the presence and absence of a test compounds (see e.g., paragraph bridging pp. 15-16), the ability of the protein to bind to its biding site on a nucleic acid or the transactivation of a gene product regulated but the Egr-1 protein." *Id.* at page 18. The Examiner also alleged that "Alberini et al. teaches methods of identifying agents that modulate the activity of an Egr-1 protein (referred to therein as ZIF268) including comparing the ability of the protein to bind to its binding site on a nucleic acid or the transactivation of a gene product regulated by the Egr-1 protein in the presence and absence of a test compound." *Id.* The Examiner concluded

that the method of each of the above documents "is the same as the method presently claimed." *Id.*

Applicants respectfully traverse. Neither of the cited documents disclose all of the claim limitations. For example, Einstein and Alberini do not discuss a step of "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." Thus, neither Einstein nor Alberini anticipate the instant claims. Applicants respectfully request withdrawal of the rejection.

Claims 1-11

Claims 1-11 were rejected under 35 U.S.C. 102(b) "as being anticipated by Rupprecht et al. (2000) *Kidney int.* 57:70-82 (hereinafter Rupprecht '00)." Action at page 18. According to the Examiner, "Rupprecht '00 teaches a method comprising comparing the expression of an Egr-1 protein in the absence (i.e., serum only) and presence of a test compound (i.e., GSNO or 8Br-cGMP)." *Id.* at page 19. The Examiner also alleged that "Rupprecht '00 teaches a method comprising comparing expression of a reporter gene under transcriptional control of Egr-1 in the absence and presence of a test compound." *Id.* The Examiner further alleged that "Rupprecht '00 teaches a method comprising comparing binding of Egr-1 to a polynucleotide and an antibody against Egr-1 (i.e., supershifting)." *Id.*

Applicants respectfully traverse. Rupprecht '00 does not disclose all of the claim limitations. Specifically, Rupprecht '00 does not disclose a step of "immobilizing on a solid phase a polynucleotide to which the protein or salt thereof is capable of binding." Accordingly, Rupprecht '00 does not anticipate the instant claims. Applicants respectfully request withdrawal of the rejection.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
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Dated: March 31, 2008

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